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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/999,690	09/08/1997	WALTER H. GUNZBURG	GSF97-03A	4218

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EXAMINER	
LI, QIAN JANICE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/999,690	GUNZBURG ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-15,20-22,26-28,30,31,34-40,46-48,52,55-65,70-72, 75,78,79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-15,20-22,26-28,30,31,34-40,46-48,52,55-65,70-72, 75,78,79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 May 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment and remarks filed on August 23, 2004 have been entered. Claims 1, 2, 5, 9, 11, 12, 20, 21, 27, 28, 31, 35, 37, 38, 46, 47, 55, 56, 58, 60, 62, 63, 70, 71 have been amended. Claims 78 and 79 are newly added. Claims 1, 2, 4-15, 20-22, 26-28, 30, 31, 34-40, 46-48, 52, 55-65, 70-72, 75, 78, and 79 are pending and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-15, 20-22, 26-28, 30, 31, 34-40, 46-48, 52, 55-65, 70-72, 75 stand rejected and claims 78 and 79 are newly rejected under 35 U.S.C. 112, first paragraph, for reasons of record and following.

In the Remark, applicants indicated that they have amended claims to replace "a part thereof, an analogue thereof, a homologue thereof" with "a biologically active peptide derived therefrom", and pointed to the support in page 9, lines 9-12 of the specification.

The amendment and remarks have been fully considered but found not persuasive, because "a biologically active peptide derived therefrom" is a variation of the previous recitation; it encompasses "a part thereof, an analogue thereof, a homologue thereof". Page 9, lines 9-12 of the specification basically recited the same term, it does not teach a consensus structure that qualifies a peptide as a "a biologically active peptide derived therefrom (having antimicrobial activity)", and it fails to teach the structure-functional correlation of "a biologically active peptide derived therefrom" so that one can determine whether a peptide belongs to this category, and it still requires undue experimentation for the skilled artisan intending to practice the invention to search through a large number of peptides that may serve as a biologically active derivatives of melittin, cecropin, magainin, a preform thereof or a preproform thereof.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-15, 20-22, 26-28, 30, 31, 34-40, 46-48, 52, 55-65, 70-72, 75 stand rejected, and claims 78 and 79 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The amended claims are vague and indefinite because the new limitation, "a biologically active peptide derived therefrom" encompasses previous claim limitation, "a biologically active derivative", "a part thereof, an analogue thereof, and a homologue thereof". One skilled in the art still do not know from the disclosure of the specification

whether a given peptide is "a biologically active peptide derived" from melittin or cecropin, it is unclear what is encompassed or excluded by these terms, thus the metes and bounds of the claims could not be readily determined.

Concerning claims 21 and 71, applicants argue it was known to one skilled in the art that DNA in a vector can be transcribed by a polymerase to produce an RNA molecule. In response, apparently as applicant indicated, the RNA is transcribed from a DNA, the DNA vector itself does not produce RNA.

Claim Objections

Claim 47 stands objected to because the word "vector" before the "recombinant" should be deleted. Applicants failed to address the objection, thus for reasons of record, the rejection stands.

Applicant is advised that should claims 2 and 5 be found allowable, claims 78 and 79 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The previous rejection of claims 1, 9, 11, 14, 15, 20, 21, 22, 26, 27, 35, 37, 40, 46, 47, 48, 52 under 35 U.S.C. 102(e) as being anticipated by *Curiel et al* (US 6,022,735), is withdrawn in view of the argument that the *Curiel et al* did not use a retroviral vector to express melittin, rather use the melittin as a test agent.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4-15, 20-22, 26-28, 30, 31, 34-40, 46-48, 52, 55-65, 70-72, 75 stand rejected, and claims 78 and 79 are newly rejected under 35 U.S.C. 103(a) as being

unpatentable over *Jaynes et al* (US 5,962,410), in view of *Gilboa et al* (US 5,658,775) and *Hodgson et al* (US 6,027,722).

In the Remarks, applicants argue it appears that none of the cited references alone teaches or suggests each and every element of the presently pending claims, that there is no motivation to combine references. Applicants argue that the level of skill in the art cannot be relied upon to provide the suggestion to combine reference.
The arguments have been fully considered but found not persuasive. The rejection under this provision is based on the combined references, and thus does not require that each reference alone teaches all the element of the pending claims. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). It appears that Applicants are arguing that the cited references do not expressly suggest the claimed invention. However, it is well established in case law that a reference must be considered not only for what it expressly teaches, but also for what it fairly suggests. In re Burkel, 201 USPQ 67 (CCPA 1979). Furthermore, in the determination of obviousness, the state of the art as well as the level of skill of those in the art are important factors to be considered. The teaching of the cited references must be viewed in light of these factors.

Moreover, *Jaynes et al* clearly taught and suggested to introduce the lytic peptides by genetically modified cells as one of the embodiment of the invention, wherein the cells were transformed with a retroviral vector comprising an expressible gene coding for the lytic peptides such as the cecropin and melittin, wherein the transfection could be conducted by electroporation, microinjection, and the like. To be

exact, "IN ANOTHER EMBODIMENT OF THE INVENTION, A LYTIC AND/OR STIMULATING PEPTIDE IS INTRODUCED INTO A HIGHER ANIMAL BY PLACING CELLS INTO THE ANIMAL WHICH HAVE AN EXPRESSIBLE GENE GENETICALLY TRANSFORMING CELLS SUCH AS BONE MARROW CELLS, EMBRYOS, HEMATOPOIETIC STEM CELLS, AND THE LIKE. TECHNIQUES FOR SUCH TRASFORMATION ARE WELL KNOWN IN THE ART AND INCLUDE, FOR EXAMPLE, TRANSFECTION WITH RETROVIAL VECTORS" (column 12, lines 42-50). Since *Jaynes et al* did not actually make the retroviral expression vector, it is necessary to turn into the state of the art with respect to the technical details, i.e. specific elements of a retroviral vector recited in the claims.

Gilboa et al and *Hodgson et al* supplemented the teaching of *Jaynes et al* by establishing that the recited specific elements are well known at the time this application was filed.

Gilboa et al teach constructing a retrovial vector (retroviral vector DNA) for producing foreign gene product in animal cells, wherein the vector comprises at least a portion of retrovirus including both the 5' retroviral LTR region and 3' LTR region containing the U3-R-U5 structure, wherein the foreign gene to be expressed is inserted in the U3 region of 3' LTR (fig. 4), wherein a polylinker cloning site is present (column 6, line 48), wherein a promoter sequence such as VIP is also present. *Gilboa et al* also teach a recombinant retroviral vector system for producing a virion and using the virion transfecting a target cell (fig. 1), such as NIH3T3 and human lymphoid cells (animal and human cells, column 11, lines 21-23).

Hodgson et al teach a 5' long terminal repeat region (LTR) comprising the U3-R-U5 structure and a 3' LTR comprising the U3-R-U5 structure, wherein the U3 is partially or completely deleted and replaced with a sequence which comprises at least one

unique restriction site (fig 2a) and at least one insertion of a heterologous DNA fragment operably linked to a promoter (figs. 4, 5). They teach the strategy of inserting foreign gene at the 3'LTR region, wherein a large deletion occurred in the U3 region and replaced by a cloning site comprising at least one unique restriction site (column 21, § 11, particularly column 21, line 67-column 22, line 4), wherein a transacting molecule (P4) could be included for regulating foreign gene expression (fig. 14)

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the retroviral vectors taught by *Gilboa et al*, and *Hodgson et al et al*, in the method of *Jaynes et al* for expressing a lytic peptide in animal cells with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because *Haynes et al* clearly taught (suggested) so, and given the numerous retroviral vectors known in the art, it is within the levels of the reasonably skilled to use an appropriate vector for expressing a gene of interest. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Apparently, the motivation used by the Office to construct this rejection is not the levels of the skilled in the art, but specific teaching and suggestion by Haynes et al. Accordingly, the rejection stands.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Amy Nelson** can be reached on 571-272-0804. The fax numbers for the organization where this application or proceeding is assigned are **703-872-9306.**

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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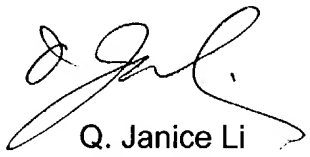

Q. Janice Li
Primary Examiner
Art Unit 1632

QJL
November 5, 2004